UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/788,974	02/26/2004	Kent Jorgensen	2081-0125P	5458

2292 7590 11/20/2008

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
11/20/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/788,974	JORGENSEN ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,9,10,12-72 and 75* is/are pending in the application.

4a) Of the above claim(s) *25-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 9-10, 12-24 and 75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 9-19-08 is acknowledged.

Claims included in the prosecution are 1-3, 9-10, 12-24 and 75.

In view of the amendments, the 112, second paragraph rejection, 103 rejections involving Hong and Peterson are withdrawn.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-3, 9-10, 14-24 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kozak (6,166,089) of record in combination with Janjic (6,229,002) and Vermehren (BBA, 1998) of record.

Kozak discloses phospholipid prodrugs wherein the carbon 1 of the glycerol has an aliphatic chain and the carbon 2 has an organic radical and carbon 3 has a phosphatidyl group. According to Kozak the organic radical is released by phospholipase A2 present in the pathological tissue (note the abstract, col. 4, line 41 through col. 11, line 9, Examples and claims).

What are lacking in Kozak are the inclusion of a lipopolymer and the administration of the composition in the form of liposomes.

Janjic while disclosing lipid constructs containing PDGF teaches the several advantages of administration of the composition in the form of liposomes and the attachment of PEG to the liposomal surface to shield the liposomal complex from blood proteins and thereby enable it to circulate for extended periods in the blood. According to Janjic, the prodrug is on the outside surface of the liposomes (note the abstract, col. 25, line 5 through col. 28, line 67).

Vermehren while disclosing liposomes containing PEG teaches that PEG not only provide steric hindrance which leads to a decrease in the adsorption and interaction of plasma degrading proteins with the liposomal surface, but also enables PLA2 to have increased catalytic activity on the phospholipid containing liposomes. Based on their studies, Vermehren suggest that one can design and optimize the in vivo degradation of drug loaded liposomes at certain sites, e.g., in extra vascular inflammatory tissue due to an enhanced local concentration of the active PLA2 and an accumulation of polymer -grafted liposomes in such tissue (note pages 31-34).

The use of polymer (PEG) containing liposomes for the delivery of the prodrug of Kozak would have been obvious to one of ordinary skill in the art because the advantages of the liposomes and the ability of PEG to prolong the circulation time of the liposomes and increasing their susceptibility to PLA2 in the host pathological tissue and thereby increasing the release of the drug attached to the carbon 2 of the phospholipid in Kozak.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues the following: "Kozak describes prodrugs with enhanced

penetration into cells. Preferably, the prodrug is a protease inhibitor conjugated to a phospholipid. According to Kozak, the protease inhibitor is preferably a calcium chelating agent. It is preferred that the prodrugs are activated by intracellular enzymes, e.g., PLA2. Kozak does not teach lipids, wherein X is 0 or S (1-position is ether or thioether), i.e., Kozak does not teach prodrugs of lyso-ether lipids. Additionally, Kozak teaches away from the present invention because, Kozak specifically teaches that it is not desirable to formulate prodrugs into liposomes since this achieves preferential distribution to specific organs and cells (Kozak, column 6, lines 4-8). Kozak does not mention that the reason why liposomes are undesirable is to avoid uptake by the RES. Kozak simply teaches that the distribution achieved using liposomes is undesirable, and the skilled person would not read this as being directed to avoidance of RES uptake. In conclusion, the skilled artisan would not combine Kozak with Vermehren or Janjic".

Applicant's argument that Kozak teaches away from formulating the prodrugs into liposomes as evident from col. 6, lines 4-6 are not persuasive since the reason for Kozak's teachings of not to use liposomes is because the liposomes are taken up by the reticuloendothelial system (RES), (liver, macrophages). However, both references of Janjic and Vermehren teach the purpose of linking PEG to the lipid (lipopolymer) that is increase in circulation time of the liposomes without being taken up by the RES. Therefore, one of ordinary skill in the art would be motivated to use liposomes in Kozak for the art known advantages of liposomes and attach PEG to the phospholipid forming the bilayer membrane of the liposomes in order to increase the circulation time of the liposomes and avoiding the RES.

These arguments are not persuasive. Kozak in example 3 clearly teaches 'O-aliphatic hydrocarbon' in carbon 1 position of the glycerol. Instant claim 1 recites, "an active selected from lysolipid derivatives, where the active drug substance is present in the lipid-based system in the form of a prodrug, said prodrug being a lipid derivative ----". This claim language does not exclude the moiety linked to the phosphate moiety in example 3 of Kozak.

3. Claims 12-13 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kozak (6,166,089) of record in combination with Janjic (6,229,002) and Vermehren (BBA, 1998) as set forth above, further in view of Saxon (Journal of Liposome Research, 1999) or Bally (5,736,155).

The teachings of Kozak, Janjic and Vermehren have been discussed above. What is lacking in Kozac, Janjic and Verneren is the administration of the composition with an additional liposome encapsulated drug.

Saxon teaches that anticancer drugs can be used in combination in liposomes (summary).

Bally similarly teaches the encapsulation of two anticancer drugs in liposomes (col. 15, Part C).

The use of an additional liposomal anticancer agent would have been obvious to one of ordinary skill in the art, with the expectation of obtaining an additional effect, since the references of Saxon and Bally show that two anticancer drugs can be used in combination.

Applicant's arguments have been fully considered, but are not persuasive. The examiner has already addressed applicant's arguments regarding Kozak. Applicant argues that though both references mention combination therapy, they does (do) not render obvious the liposomal delivery system. This is not persuasive since as recognized by applicants themselves, these references are combined for the use of combination therapy using the liposomal systems. With regard to the unexpected results, the examiner points out that the properties of the lyso-ether lipids and liposomes are well known and Kozak teaches the release of the organic radical by the phospholipase A2 present in the pathological tissue just as in instant invention.

4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore/
Primary Examiner, Art Unit 1612

GSK